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Application No.	Ref.	Date
04 809 859.4 - 2107	PCB/P05411PEP	31.10.2008
Applicant: Cedars-Sinai Medical Center		

Communication pursuant to Article 94(3) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(2) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 126(2) and 131(2) and (4) EPC. One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (R. 50(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Art. 94(4) EPC).

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Greif, Gabriela
Primary Examiner
For the Examining Division

Enclosure(s): 4 page/s reasons (Form 2906)

The examination is being carried out on the **following application documents**:

Description, Pages

1-26 as published

Claims, Numbers

1-12 received on 28.03.2006 with letter of 23.03.2006

Drawings, Sheets

1/6-6/6 as published

1. Art. 84 EPC

1.1. Further medical use claim 1 "a disease condition in a mammal that requires administration of at least one vaccination of dendritic cells to said mammal" is not acceptable under Article 84 EPC. The therapeutic application is functionally defined by a mechanism of action which does not allow any practical application in the form of a defined, real treatment of a pathological condition (disease) (C-IV, 4.8).
The objection could be overcome by either introducing into the claims a list of pathological conditions (diseases) cited in the application, or incorporating the disease of claims 6 or 7 in claim 1, or by showing that means are available which would allow the skilled person to recognise which additional conditions would fall within the functional definition (C-III, 6.5).

1.2. Present claims 1-4 and 6-12 are not clear, their subject-matter is defined by means of a functional feature: " "cyclooxygenase-2 inhibiting compound". Because of the character of the functional feature, it cannot be excluded that compounds fulfilling the requirements of the functional feature have not been identified as

doing so in the prior art. If such compounds have not been identified in the application either, they have not been covered by the search. Although the wording of the functional feature per se is clear, said wording does nevertheless not allow to clearly determine which compounds fall under said definitions. Concerning said claims, an opinion will only be established with respect to the compounds disclosed in claim 5, others that are identified in the application documents, as well as the general term per se.

1.3. The term "vaccination of dendritic cell" is not clear, since its wording might imply that the dendritic cells are somehow treated in order to be vaccinated, which is another level of lack of clarity, or that their administration in addition with the COX-2 inhibitor (see also claim 12) represents the vaccination. In this respect, the presence of dendritic cells in the body (untreated) in addition of an administered COX-2 inhibitor is according to the wording of the claim reflecting the circumstances of the use. The wording of claim 1 does not imply that the vaccination of dendritic cells (whatever it is) actually takes place, it just uses the term to define the condition. In essence, the parts of the claims that are clear and supported by the description relate to the treatment of specific cancers by COX-2 inhibitors.
In this context, claim 12 is unclear, since it implies the administration of dendritic cells.

2. Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure:

D1: MATASIC R ET AL: "Cyclooxygenase-independent inhibition of dendritic cell maturation by aspirin." IMMUNOLOGY SEP 2000, vol. 101, no. 1, September 2000 (2000-09), pages 53-60

D2: HARIZI HEDI ET AL: "Prostaglandin E2 modulates dendritic cell function via EP2 and EP4 receptor subtypes." JOURNAL OF LEUKOCYTE BIOLOGY JUN 2003, vol. 73, no. 6, June 2003 (2003-06), pages 756-763

D3: SHENG H. ET AL.: 'Inhibition of human colon cancer cell growth by selective inhibition of cyclooxigenase-2.' J. CLIN. INHIB. no. 9, May 1997, pages 2254 - 2259

D4: FERRANDINA G. ET AL.: 'Celecobix modulates the expression of cyclooxigenase -2,Ki67 apoptosis-related marker, and microvessel density in human cervical cancer.' CLIN.CANCER RES. vol. 9, 01 October 2003, pages

4324 - 4331

D5: ABIRU S. ET AL.: 'Aspirin and NS-398 inhibit hepatocycle growth factor-induced.' HEPATOLOGY. vol. 35, 2002, pages 1117 - 1124

D6: EHTESHAM M ET AL: "Intratumoral dendritic cell vaccination elitics potent tumroicidal immunity against malignant glioma in rats" JOURNAL OF IMMUNOTHERAPY, LIPPINCOTT WILLIAMS & WILKINS, HAGERSTOWN, MD, US, vol. 26, no. 2, March 2003 (2003-03), pages 107-116,

D7: YU J S ET AL: "Vaccination of malignant glioma patients with peptide-pulsed dendritic cells elicits systemic cytotoxicity and intracranial T-cell infiltration" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 61, no. 3, 1 February 2001

D8: ZITVOGEL L. ET AL.: 'Therapy of murine tumors with tumor peptide-pulsed dendritic cells: dependence on T cells, B7 constimulation, and helper cell-1 associated cytokines.' J. EXP.MED. vol. 183, January 1996, pages 87 - 97,

3. Novelty

D1 states on p. 59, left column, last paragraph that aspirin or salicylates inhibit NF-kappaB function in dendritic cells and inhibit dendritic cell differentiation with loss of immunostimulatory function, thus reduce inflammation in vivo and treat autoimmunity (also the whole document). Taking into account the lack of clarity of claim 1, it would appear that the subject-matter of claims 1-4,8, and 9 lack novelty over D1.

D2 states that dendritic cell function is modulated by the COX-2 inhibitor NS-398, and discloses a composition comprising dendritic cells and NS-398 (fig. 1). Claim 12 thus lacks novelty over D2.

D3 states that COX-2 is expressed in high levels in intestinal tumours, and that the treatment of tumors with the COX-2 inhibitor SC-58125 resulted in a reduction of tumor formation in a tumor cell line (abstract). Claims 1-4, 6, and 8-10 thus lack novelty over D3, especially since the subject-matter of claims 8 and 9 represents an inherent property of the active agent.

D4 studies the effect of COX-2 inhibitor celexocib in human cervical cancer cells, and states that selective COX-2 inhibitors may be a promising strategy for therapeutic treatment of such cancers (abstract). Claims 1-4 and 8-9 lack novelty over D4.

D5 states that COX-2 inhibitors are effective in the inhibition of invasiveness of hepatoma cells, and study the mechanism of action of the COX-2 inhibition,

suggesting that the ERK1/2 pathway is involved (the whole document). Claims 1-4 as well as 8-9 are considered not novel over D5, since again the mechanism of action of the compounds is considered an inherent property.

4. Inventive Step

If the applicant would obviate the novelty objections the following is to be noted with respect to inventive step:

As a consequence of the clarity objections, it would appear that the claims of the present application relate to the treatment of cancers according to claims 6 and 7 by the use of COX-2 inhibitors like NS-398.

Claim 12 appears to suggest the combination of a dendritic cell (considered as a vaccine) and a COX-2 inhibitor for use as a medicament.

D2 states that COX-2 issued PGE2 is able to modulate dendritic cell function through stimulation of specific EPR subtypes, resulting in an immunosuppressive and antiinflammatory effect (abstract, p. 760, right column, discussion). Thus, the expert learns that DC function can be influenced by the administration of COX-2 inhibitors.

D6-D8 all disclose treatment of various cancers like gliomas by vaccination with dendritic cells. From these documents, the expert in the field would derive the use of COX-2 inhibitors being able to manipulate DC function, and their use in cancers like gliomas.

5. It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 43(1) EPC. The applicant should also indicate how the subject-matter of the new claim differs from the state of the art and the significance thereof.